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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

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Washington, DC 20460

EPA Pesticide Fact Sheet

Name of Chemical: Acephate
Reason for Issuance: Issuance of a Registration Standard
Date Issued: 10/87
Fact Sheet Number: 140

1. Description of Chemical

Generic Name: O,S-dimethyl acetylphosphoramidothioate
Common Name: Acephate
Trade Name: Orthene
EPA Shaughnessy Code: 103301
Chemical Abstracts Service (CAS) Number: 30560-19-1
Year of Initial Registration: 1974
Pesticide Type: Insecticide
Chemical Family: Organophosphate
U.S. and Foreign Producers: Chevron Chemical Co. (U.S.A.)

2. Use Patterns and Formulations

Application Sites: Agricultural crops; ornamentals (field grown, greenhouse, and home garden); lawns and turf; pasture and rangeland; forestry; indoor homeowner use on houseplants; and commercial applicator use in residential and commercial buildings including food processing establishments.

Types and Methods of Application: Aerial; ground; direct injection into tree trunks; dip treatment (ornamentals); soil incorporated; and sprinklers.

Type of Formulations: Granular, pressurized liquid, soluble concentrates (both liquids and solids), and cartridge.

3. Science Findings

Summary Science Statement: Acephate has a relatively low acute toxicity to laboratory animals through the oral, dermal, and inhalation routes of exposure. Based on the available evidence, i.e., findings from the mouse oncogenicity study, and the mutagenicity assays, the Agency has classified the chemical as a category C carcinogen (a possible human carcinogen). The mouse oncogenicity study indicated a statistically significant increase in the proportion of liver adenomas/carcinomas and hyperplastic nodules occurred only in the high dose (1000 ppm) females and only at the time of terminal sacrifice. The EPA Guidelines for carcinogenic

risk assessment (FR September 24, 1986) were followed for the evaluation and the classification of the oncogenic effect of acephate. Following the guidance set forth in the EPA guidelines, the mouse oncogenic response was considered as "limited evidence."

The available data are not sufficient to enable the Agency to accurately assess the potential risk to humans from this oncogenic effect resulting from exposure to acephate. The data gaps include residue reduction studies, exposure studies, usage data, a dermal penetration study, a glove permeability study, and reentry data.

The available rat reproduction study showed reproductive effects at 50.0 ppm, the lowest dose tested. A new rat reproduction study is needed to determine the no-observable-effect level (NOEL) for these effects and to enable the Agency to assess the potential risk to humans resulting from exposure to acephate.

Methylthioacetate (MTA) occurs as an impurity in the current registered technical material. The available data suggest that the MTA, despite its generally low acute toxicity, may pose a hazard to the optic tract and pituitary gland in rabbits and other mammals at low doses. Data were not provided to demonstrate a NOEL for lesions at these target organs. Since visual impairment is inherently difficult to diagnose in animals, it is possible that this effect occurred in other studies but was not detected. In addition, a mutagenic effect was seen in the mouse lymphoma assay in the activated system. Due to the insufficiency of the submitted data to explain the toxic and mutagenic potential of MTA, the Agency requires that additional studies be performed.

Methamidophos, the cholinesterase-inhibiting metabolite of acephate, is also an insecticide in its own right, and as such, was assessed under a separate Registration Standard issued for the chemical in September 1982. Several of the data gaps identified in that standard have been fulfilled. It is highly toxic by both the oral and dermal routes (Toxicity Category I). Results of two oncogenicity studies show that methamidophos was not oncogenic in rats at dose levels of 2,6,18 and 54 ppm nor in mice at dose levels of 1,5,and 25 ppm. The available teratogenicity studies show that it is not teratogenic to rats or rabbits. The chemical was negative for acute delayed neurotoxicity in the submitted study on hens. The lowest effect level (LEL) for cholinesterase inhibition activity was determined to be 2 ppm (0.05 mg/kg/day) in both the 1-year dog study and the 2-year rat study.

Data gaps for methamidophos include a rat reproduction study and mutagenicity studies.

Chemical Characteristics

Physical State: Solid
Color: White
Odor: Strong, pungent, mercaptan-type
Boiling Point: N/A

Melting Point: 82-89 °C (97% technical)
Flammability: N/A
Solubility in Water: High solubility (65%)

Toxicology Characteristics:

ACEPHATE:

- Acute Oral - Rat: 945 mg/kg (male); 866 mg/kg (female)
  Toxicity Category III

- Acute Dermal - Rabbit: > 10,000 mg/kg (male)
  Toxicity Category III

- Acute Inhalation - Rat: > 61.7 mg/kg (male and female)
  Toxicity Category IV

- Acute Delayed Neurotoxicity - Hen: Negative at 785 mg/kg of body weight

- Mouse Oncogenicity: Female mice fed 1000 ppm of technical acephate (highest dose tested) had a statistically significant higher incidence of hepatocellular carcinomas (15.8%) and hyperplastic nodules (19.7%) than did the controls.

- Rat Oncogenicity: Not oncogenic to male and female rats under the conditions of the study; highest dose tested was 700 ppm (35 mg/kg).

- Rat Chronic Feeding: LEL = 5 ppm (0.25 mg/kg) based on the inhibition of cholinesterase activity in plasma, RBC, and brain.

- Dog Chronic Feeding: NOEL = 30 ppm (0.75 mg/kg) based on the inhibition of plasma, RBC, and brain cholinesterase activity. NOEL = > 100 ppm (2.5 mg/kg) for systemic toxicity.

- Rabbit Teratogenicity: Not fetotoxic or teratogenic at 10 mg/kg (highest dose tested).

- Rat Teratogenicity: Not teratogenic at 200 mg/kg (highest dose tested).

- Mutagenicity: The available studies indicate that acephate can induce gene mutations, DNA repair, and sister chromatid exchanges. However, in vivo studies did not indicate that these effects and structural chromosome aberrations are produced at a detectable level in an intact mammalian system.

- Rat Reproduction: Various reproductive effects (low pregnancy rate, high loss of total litters, high fetal losses, decreased size and weight of total litters, and decreased number of live fetuses) were observed at the lowest dose level tested, which was 50.0 ppm of technical acephate (93% acephate).

METHYLTHIOACETATE (MTA):

- Acute Dermal - Rabbit: 1720-2820 mg/kg; Toxicity Category II-III. Clinical signs included irreversible absence/diminution of pupillary light reflex and apparent blindness.
- Acute Inhalation - Rat: 3.47 mg/L; Toxicity Category III.
- Skin Irritation - Rabbit: 2.6 Primary Irritation Score; Toxicity Category III.
- Skin Sensitization - Guinea Pig: Nonsensitizing and nonirritating; dose level tested was 0.3 ml (0.3 g).
- Eye Irritation - Rabbit: Toxicity Category III; dose level tested was 0.1 mL of 93.5% MTA.
- Mutagenicity - Mouse Lymphoma Assay: Mutagenic to lymphoma cells in the activated system but not in the nonactivated system; levels tested were 1-10,000 ug/ml (activated) and 10-5000 ug/ml (nonactivated).

Physiological and Biochemical Behavioral Characteristics:

Translocation: The available plant metabolism studies show that acephate residues are readily absorbed by the roots and translocated throughout the plant. However, data show that acephate does not accumulate in carrot plants rotated in acephate-treated soil or in fish, daphnia, or diatoms.

Mechanism of Pesticidal Action: Acephate is a contact and systemic insecticide. As an organophosphate, acephate exerts its toxic action by inhibiting certain important enzymes of the nervous system (cholinesterase).

Metabolism and Persistence in Plants and Animals: The metabolism of acephate in plants and animals is adequately understood. Available data show that the residues in or on plants resulting from acephate use may be largely or wholly intact acephate and its metabolite, methamidophos. Available animal metabolism data show that most of the radiolabeled material is rapidly eliminated from the body and that a majority of the material is excreted in the urine.

Methamidophos is not the major metabolite in ruminants. About 80 percent of the radiolabeled material in the urine was associated with unchanged acephate and less than 10 percent with the metabolite O,S-dimethylphosphorothioate. Most of the methamidophos formed is probably eliminated and excreted in the urine as O,S-dimethylphosphorothioate.

Environmental Characteristics:

Due to its rapid leaching behavior, acephate has the potential for ground water contamination. Available data are insufficient to fully assess this potential. Pertinent data (mobility, photodegradation, metabolism, and dissipation) are being required under the Acephate Registration Standard on an accelerated basis.

Available soil metabolism studies show that acephate dissipates rapidly with half-lives of < 3 and 6 days in aerobic and anaerobic soils, respectively. The major metabolite was CO_2 in both types of soil. The available leaching data include a soil thin-layer chromatography (TLC) study and a soil column study. Results of these studies indicate that acephate is mobile in most soils but that aged acephate residues (excluding acephate and its degradate methamidophos) are immobile in sandy loam soil. Apparently most of the applied acephate and the degradate methamidophos degrade to immobile compounds in 20 days.

Ecological Characteristics:

- Avian Oral Acute Toxicity: 350 mg/kg (mallard) and 140 mg/kg (pheasant)
- Avian Dietary Toxicity: > 5000 ppm (mallard) and 1280 ppm (bobwhite)
- Fish Acute Toxicity: > 1000 ppm (rainbow trout) and > 1000 ppm (bluegill sunfish)
- Freshwater Invertebrate Acute Toxicity: > 1000 ppm (Chironomus) and > 100 (Gammarus)
- Avian Reproduction: NOEL = > 5 ppm but < 20 ppm for mallard and NOEL = > 20 ppm but < 80 ppm for bobwhite.
- Honey Bee Acute Toxicity: 1.2 ug/bee.

Based on these studies, acephate is moderately toxic to avian species, practically nontoxic to freshwater fish and freshwater invertebrates, and highly toxic to honey bees.

However, acephate's metabolite, methamidophos, has been shown to be very toxic to birds. Therefore, additional testing (residue monitoring studies) are being requested to complete a hazard assessment for the multiple-application, high-use rate field crops. Appropriate labeling for the protection of endangered species determined to be in jeopardy from use of acephate on forests, range and pastureland, soybeans, and cotton have been developed by the Agency and were imposed under PR Notices 87-4 and 87-5.

Tolerance Assessment:

Refer to Attachment A for the list of currently established tolerances for acephate as well as the tolerance changes to be initiated by the Agency.

To achieve compatibility with the maximum residue levels of the Codex Alimentarius Commission, the following revisions in 40 CFR 180.108, 21 CFR 561.20, 40 CFR 180.315, 21 CFR 561.277, and 21 CFR 193.10 are to be initiated by the Agency.

- 40 CFR 180.108 and 21 CFR 561.20

  The acephate tolerances currently established under these sections are to be expressed in terms of only acephate *per se*, with references to 40 CFR 180.315 and 21 CFR 561.277 indicating that tolerance for the metabolite methamidophos are also in effect.

- 40 CFR 180.315 and 21 CFR 561.277

  The methamidophos tolerances currently established under these sections are to be divided into parts (a) and (b) where (a) includes (1) tolerances reflecting uses of methamidophos and (2) tolerances where both acephate and methamidophos formulations are used on the same crop and (b) includes tolerances reflecting uses of acephate formulations alone, i.e., residues of methamidophos resulting from the metabolism of acephate.

- 21 CFR 193.10

  These food additive tolerances reflecting crack and crevice treatment in food-handling facilities are to be expressed in terms of only acephate *per se*, i.e., based on the available data. No residues of the metabolite methamidophos are expected to occur (< 0.001 ppm) in or on these foods.

Also, such a change in the residue definition would require deletion of the paragraph (d)(8) of 40 CFR 180.3, which states that methamidophos residues may not exceed the higher of the two tolerances established for the use of acephate or methamidophos as a pesticide.

The tolerance for acephate residues in milk has been found likely to be exceeded if maximum levels of spent mint hay or grass hay are included in the dairy animal diet. Labeling restrictions prohibiting the feeding of spent mint hay and grass hay to dairy animals are being imposed under this Standard for the use of acephate on pasture, rangeland, peppermint, and spearmint. If the registrant elects to submit additional residue data to support a lower tolerance for grass and grass hay, or to support a longer pregrazing or preharvest interval for dairy animals, the labeling restriction for use on pasture and rangeland would be imposed as an interim precautionary measure pending submittal and evaluation of these data.

Available data are not sufficient to conduct a full tolerance assessment. Data gaps exist for magnitude of residue studies, residue storage stability studies, a dairy cattle feeding study, a rat reproduction study, and a rat feeding study.

4. Summary of Regulatory Position And Required Unique Labeling

Registration of current registered uses of acephate is to be continued. Additional data to allow the Agency to better define the dietary, occupational, and domestic exposure risks from the registered uses of the chemical are being required. Once the Agency has evaluated these data, it will determine whether the chemical should be placed in Special Review or returned to the normal registration process. Pending submittal and evaluation of these data, no additional tolerances, including temporary tolerances, will be established for acephate and no new uses will be registered, i.e., uses that would result in an increase in the current exposure to humans or in new exposure to humans.

As interim measures to reduce exposure pending submittal and evaluation of the additional studies specified above, the following restrictions are being imposed or, in the case of the last restriction concerning domestic use, continued: A reentry interval of 24 hours for fieldworkers; the use of protective clothing, including chemical-resistant gloves, long-sleeved shirts and long-legged trousers, shoes and socks by mixer/loaders, applicators, and early reentry workers who may be exposed to treated plant surfaces within 24 hours of acephate application; dairy animal feeding restrictions as described above under Tolerance Assessment; and, for domestic use, the restriction not to allow children or pets on treated surfaces until sprays have dried.

The 24-hour reentry interval is being imposed for the use of acephate on agricultural crops, commercially grown ornamentals, in commercial or governmental forestry seed production, and in greenhouses.

As described above under Ecological Characteristics, the Agency has imposed labeling restrictions for the protection of endangered species determined to be in jeopardy from use of acephate.

5. Summary of Major Data Gaps

Toxicology	Date Due
- Acephate	
Rat Reproduction	39 Months
21-Day Inhalation	6 Months (Protocol)
Rat Feeding Study	6 Months (Protocol)
- Methylthioacetate (MTA)	
Acute Oral (Rat and Rabbit)	9 Months
Acute Dermal (Final Report - Rabbit)	9 Months
Acute Inhalation	9 Months
90-Day Dermal (Rabbit)	15 Months
Mutagenicity	12 Months
Environmental Safety	
Avian Residue Monitoring	6 Months (Protocol)
Environmental Fate	
Soil Photodegradation	9 Months
Anaerobic Aquatic Metabolism	27 Months
Adsorption/Desorption	12 Months
Soil Dissipation - Field	27 Months
Irrigated Crop	39 Months
Confined Rotational Crop	39 Months
Spray Drift	6 Months
Exposure	
Applicator (Outdoor and Indoor)	6 Months (Protocol)
Indoor Inhabitants	6 Months (Protocol)
Glove Permeability	6 Months (Protocol)
Residue Chemistry	
Storage Stability	24 Months
Magnitude of Residues	24 Months
Dairy Cattle Feeding	18 Months
Tobacco Residue	24 Months

Benefits

Usage	6 Months
Use-Related Exposure	6 Months

6. Contact Person at EPA

William H. Miller (PM 16)
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Washington, DC 20460.

DISCLAIMER: The information presented in this Chemical Information Fact Sheet is for informational purposes only and may not be used to fulfill data requirements for pesticide registration and reregistration.

Attachment A

Tolerance Changes Reflecting the Recommended Change in Residue Definition

Commodity	Acephate*		Methamidophos	
	Established Tolerance (ppm)[a]	Recommended Tolerance (ppm)[b]	Established Tolerance (ppm)[c]	Recommended Tolerance (ppm)[c]
Beans (succulent and dry forms)	3(1)	3	---	1
Brussels sprouts	3(0.5)	3	1	1
Cauliflower	2(0.5)	2	1	1
Celery	10(1)	10	1	1
Cottonseed	2	2	0.1	0.5
Cranberries	0.5(0.1)	0.5	---	0.1
Eggs	0.1	0.1	---	0.01
Fat, meat, and meat byproducts[d]	0.1	0.1	---	0.01
Grass (pasture and range)	15	15	---	3
Grass hay	15	15	---	3
Lettuce (head)	10(1)	10	1[e]	1
Milk	0.1	0.1	---	0.05
Mint hay	15(1)	15	---	1
Peanuts	0.2	0.2	---	0.1
Peanuts hulls	5	5	---	1.5
Peppers	4(1)	4	1[f]	1
Soybeans	1	1	---	0.2
Cottonseed hulls[g]	4	4	---	0.1
Cottonseed meal[g]	8	8	---	2.5
Soybean meal[g]	4	4	---	2
Processed foods[h]	0.02	0.02	---	---

[a] Expressed in terms of combined residues of acephate and methamidophos. If specified, limits of methamidophos are given parenthetically.

[b] Expressed in terms of acephate per se only.

[c] Expressed in terms of only methamidophos per se.

[d] Included are cattle, goats, hogs, horses, poultry, and sheep.

[e] The methamidophos tolerance covers all types of lettuce (head and leaf).

[f] The methamidophos tolerance covers all types of peppers.

[g] Feed additive tolerances in 21 CFR 561.20 (acephate) and recommendations for inclusion under 21 CFR 561.277 (methamidophos).

[h] Food additive tolerance reflecting spot and crack and crevice treatment of food areas of food handling establishments (21 CFR 193.10). There is no expectation of methamidophos residues in such foods (residues were nondetectable, < 0.001 ppm, in all cases).

* This table does not include the tolerance of acephate in/on macadamia nuts (.05 ppm), which was established subsequent to completion of the evaluation needed for this Document. Acephate is not currently registered for use on macadamia nuts.